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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,943	09/16/2003	Rolland F. Hebert		3862

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EXAMINER	
LEWIS, PATRICK T	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,943	HEBERT, ROLLAND F.	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03082004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 14-18 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method to treat a condition of lowered S-adenosyl-1-methionine tissue and blood levels comprising administering to an animal in need thereof an effective amount of a substantially optically pure (S,S)-S-adenosyl-1-methionine or a pharmaceutically acceptable salt thereof or a defined non-racemic ratio of (S,S)-adenosyl-1-methionine to (R,S)-adenosyl-1-methionine or pharmaceutically acceptable salts thereof, does not reasonably provide enablement for a method to prevent a condition of lowered S-adenosyl-1-methione tissue and blood levels comprising administering to an animal in need thereof an effective amount of a substantially optically pure (S,S)-S-adenosyl-1-methionine or a pharmaceutically acceptable salt thereof or a defined non-racemic ratio of (S,S)-adenosyl-1-methionine to (R,S)-adenosyl-1-methionine or pharmaceutically acceptable salts thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which it pertains to make and use the invention as of its filing date, *In re Glass*, 181 USPQ 31; 492 F2.d 1228 (CCPA 1974). The essence of the invention, must be described in such details, including proportions and techniques where necessary, as to enable those persons skilled in the art to make and utilize the invention. Applicant asserts conditions such as aging, Alzheimer's disease, HIV/AIDS, bile dysfunction, acute and chronic liver disease, strokes, Parkinson's disease, pain, and memory loss are prevented by employing the instantly claimed method. Applicant does not provide an adequate written description which provides guidance for the use of S-adenosyl-1-methionine (optically pure or isomeric mixture) for preventing a condition of lowered S-adenosyl-1methionine tissue and blood levels. There are no teachings or suggestions in the prior art or instant disclosure that would lead one of ordinary skill in the art to conclude that said conditions are prevented by the instant method.

3. Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A disclosure in an application, to be complete, must contain such description and details as to enable any person skilled in the art or science to which it pertains to make and use the invention as of its filing date, *In re Glass*, 181 USPQ 31; 492 F2.d 1228 (CCPA 1974). The essence of the invention, must be described in such details,

including proportions and techniques where necessary, as to enable those persons skilled in the art to make and utilize the invention. Applicant asserts conditions such as aging, Alzheimer's disease, HIV/AIDS, bile dysfunction, acute and chronic liver disease, strokes, Parkinson's disease, pain, and memory loss are prevented by employing the instantly claimed method. Applicant does not provide an adequate written description which provides guidance for the use of S-adenosyl-1-methionine (optically pure or isomeric mixture) for preventing a condition of lowered S-adenosyl-1methionine tissue and blood levels. There are no teachings or suggestions in the prior art or instant disclosure that would lead one of ordinary skill in the art to conclude that said conditions are prevented by the instant method.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 14-19 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gennari US 4,465,672 (Gennari) and De La Cruz et al. Naunyn-Schmiedeberg's Archives Pharmacology (2000), pages 47-52 (De La Cruz) in combination.

Claims 14-19 and 21-23 are drawn to a method to treat or prevent a condition of lowered S-adenosyl-1-methionine tissue and blood levels comprising administering to an animal in need thereof an effective amount of a substantially optically pure (S,S)-S-adenosyl-1-methionine or a pharmaceutically acceptable salt thereof or a defined non-racemic ratio of (S,S)-adenosyl-1-methionine to (R,S)-adenosyl-1-methionine or pharmaceutically acceptable salts thereof. Claims 15-18 limit the ratio of (S,S)-S-adenosyl-1-methionine in the pharmaceutical composition. Claims 19 and 22 limit the condition treated. Claim 21 limits the mode of administration. Claim 23 limits the pharmaceutically acceptable salt.

Gennari teaches that S-adenosyl-1-methionine (SAM) participates in a great number of metabolic processes of fundamental importance for the human organism, and consequently it deficiency lies at the basis of many organic malfunctions (column 1, lines 10-65; column 2, lines 33-62). Although the biological importance of this product has been known for some decades, the possibility of testing it and thus using it as a drug has existed only in recent years, because of its extreme instability at temperatures exceeding 0° C. It has now been found that stable SAM salts are obtained whenever SAM is salified with 5 moles of an organic sulphonic acid of pK less than 2.5. A particularly useful salt is p-toluenesulphonic acid. Gennari teaches salts intended for

use in injectable pharmaceutical forms and oral tablets (column 3, lines 45-51). The activity of the new products have been clinically established in hepatology in the case of acute and chronic hepatic intoxication, in neurology as an antidrepressive, and in osteology in the case of rheumatoid arthritis (column 9, lines 26-34).

Gennari differs from the instantly claimed method in that: 1) Gennari does not teach the use of a substantially optically pure (S,S)-S-adenosyl-1-methionine or a pharmaceutically acceptable salt thereof or a defined non-racemic ratio of (S,S)-adenosyl-1-methionine to (R,S)-adenosyl-1-methionine or pharmaceutically acceptable salts thereof and; 2) Gennari does not teach a method to treat a condition of lowered antioxidant levels.

De La Cruz teaches the SAM is used to treat liver diseases, as a coadjuvant in antidepressive medications, and has neuroprotective effects in animals. De La Cruz further teaches that SAM shows characteristics of an antioxidant drug and may be able to protect the brain from oxidative damage (page 47).

It would have been obvious to one of ordinary skill in the art at the time of the invention to treat a condition of lowered S-adenosyl-1-methionine tissue and blood levels (including oxidative damage of the brain) by administering to an animal in need thereof an effective amount of a substantially optically pure (S,S)-S-adenosyl-1-methionine or a pharmaceutically acceptable salt thereof or a defined non-racemic ratio of (S,S)-adenosyl-1-methionine to (R,S)-adenosyl-1-methionine or pharmaceutically acceptable salts thereof. Although the prior art does not explicitly teach the ratio of the (S,S) vs. (R,S) isomer, SAM is known in the art to treat conditions of lowered S-

adenosyl-1-methionine tissue and blood levels. The optimization of the (S,S) vs. (R,S) ratio of the prior art composition is seen to be well within the purview of the skilled artisan, as the separation of (S,S)-adenosyl-1-methionine and (R,S)-adenosyl-1-methionine was known in the art at the time of the invention. It is widely known in the pharmaceutical arts that the biological activity of compositions containing stereoisomers is often due to the presence of one isomer versus another. One of ordinary skill in the art would have been motivated to optimize the isomeric ratio in order to reduce the amount of therapeutic agent administered during treatment and to reduce possible side effects associated with the non-active isomer(s).

Conclusion

7. Claims 14-23 are pending. Claims 14-23 are rejected. No claims are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623

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